UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,383	12/05/2003	Keith Graham Packham	674519-2029	9236

20999 7590 09/30/2005

FROMMER LAWRENCE & HAUG
745 FIFTH AVENUE- 10TH FL.
NEW YORK, NY 10151

EXAMINER	
O HARA, EILEEN B	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 09/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/728,383	PACKHAM ET AL.	
	Examiner	Art Unit	
	Eileen O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2005 and 30 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,6,10-36 and 41-43* is/are pending in the application.

4a) Of the above claim(s) *33-36 and 41-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5, 6 and 10-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,5,6,10-36 and 41-43* ~~are~~ were subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 5, 6, 10-36 and 41-43 are pending in the instant application. Claims 2-4, 7-9 and 37-40 have been canceled and claims 1, 5 and 6 have been amended as requested by Applicant in the Paper filed June 30, 2005.

Election/Restrictions

2. Applicant's election of Group I in the reply filed on June 30, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 33-36 and 41-43 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. XX.

Claims 1, 5, 6 and 10-32 are currently under examination.

Withdrawn Objections and Rejections

3. Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

Oath/Declaration

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because:
> It does not identify the city and either state or foreign country of residence of each inventor. The residence information may be provided on either on an application data sheet or supplemental oath or declaration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5.1 Applicants on pages 10-11 of the response traverse the rejection of claims directed towards a method of treatment. These claims are withdrawn, so the rejection is also withdrawn, but Applicants' arguments will be addressed, because they are relevant to the following rejections. Applicants assert that according to the Office Action, in order to obtain claims directed towards a method of treatment, one would have to present a patent application containing results from *in vivo* human trials. Applicants submit U.S. Patent No. 5,281,587, wherein method of treatment claims were allowed without the presence of *in vivo* human examples. Also argued is that in vitro testing of compounds on human cancer cells is widely taught and is accepted in the art as a suitable alternative to widescale testing of compounds in humans, and present the paper by Voskoglou-Nomikos et al., wherein it was determined through

a retroactive review of the literature that *in vitro* cell line models were predictive of clinical results.

Applicants' arguments have been fully considered but are not deemed persuasive. While it is true that *in vivo* data is not required to satisfy the enablement requirement, there are many factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (FED. Cir. 1988).

All the Wands factors are considered and it is the balance of factors that determines whether a disclosure enables the use of the invention. In the previous Office Action, all of these factors were considered.

The MPEP states in section 2164.02:

"Lack of a working example, however, is a factor to be considered, especially in a case involving an unpredictable and undeveloped art."

In the instant case, an *in vitro* system of inhibiting growth of tumor cells is not predictive of a method of treatment, for the reasons discussed in the previous Office Action on pages 7-8. Because of the complexity of biological systems and hormone regulation, an *in vitro* system of inhibiting growth of tumor cells is not sufficiently enabling for claims directed to methods of treatment of subjects. Voskoglou-Nomikos et al., state at the end of the abstract: "These results suggest that under the right framework and when panels are used, the *in vitro* cell line and human

xenograft models ***may*** be useful in predicting the Phase 11 clinical trial performance of cancer drugs.

Additionally, *in vivo* studies of the EMATE of the instant invention have demonstrated that estrogen levels are actually increased and not decreased after administration of EMATE, so that treating estrogen-dependent tumors is counter-indicated.

Kasch et al., U.S. Patent No. 6,339,079, teaches at column 1, lines 27-40:

"Recently, it was found by M. J. Reed, et al. [Biochemistry 34 (1995) 11508-11514; J. Steroid Biochem. Molec. Biol. 57 (1996) 79-88] that a strong sulfatase-inhibiting activity is exerted by estradiol- and estrone-3-sulfamates. Sulfatase inhibitors can be used to treat estrogen-dependent tumors in that they prevent the release of estradiol or estrone from endogenic steroid conjugates, i.e., the corresponding sulfates. It was subsequently indicated that steroidal sulfatase inhibitors of the estradiol- or estrone-3-sulfamate type can be used only conditionally as sulfatase inhibitors for treating estrogen-dependent tumors. In *in vivo* experiments, these compounds show an increased estrogenic activity [Elger, W., et al., J. Ster. Biochem. Molec. Biol. 55 (1995) 395-403] which is undesirable in this indication."

Also, see last paragraph of Elger et al.

Therefore, the *in vitro* data presented in the specification was clearly not predictive of *in vivo* effect.

5.2 Claims 1, 5, 6, 10-20, 22, 23 and 25-32 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants traverse the rejection at pages 7-8 of the response, and submit that the amended claims require that the sulphamate is a polycyclic compound and that the apoptosis inducer is a tumor necrosis factor apoptosis inducing ligand, and that these recitations are sufficiently descriptive and are sufficiently decribed within the specification, such that one of skill in the art would understand that the inventors had possession of the invention at the time of filing. Applicants also assert that issued claims of Patent 6,676,934 recite "a polycyclic sulphamate compound", and in issuing the claims, the Patent Office asserted that the tern did not suffer from a lack of written description.

Applicants' arguments have been fully considered but are not deemed persuasive. The only compounds disclosed as having the disclosed activities are (EMATE), 2-meothxy oestrone-3-O-sulphamate (2-MeO EMATE), 2 ethyloestrone-3-O-sulphamate (2-EtEMATE), and 2-meothxyoestrone-3-O,17-bissulphamate (2-MeO2bis EMATE), which all comprise the same steroid ring structure and all of which have the same sulfamate group attached to the 3 position of the A ring. No other polycyclic compound has been disclosed. With the exception of the highly analagous compounds EMATE, 2-MeO EMATE, 2 EtEMATE, and 2-MeO2bis EMATE, the skilled artisan cannot envision the detailed structure of the claimed sulphamate compounds and the apoptosis inducers, regardless of the complexity or simplicity of the method of identifying the compounds. As a result, it does not appear that the inventors were in possession of the invention to use all sulphamates set forth in the claims. In response to Applicants arguments that issued claims of Patent 6,676,934 recite "a polycyclic sulphamate compound", each application is examined on its own merits.

5.3 Claims 1, 5, 6 and 10-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 1, 5, 6, 10-36 and 41-43 are drawn to a composition comprising a polycyclic sulfamate compound and a ligand that binds TRAIL-R1 of TRAIL-R2.

The instant specification discloses a number of experiments in which it is demonstrated that the analogous compounds EMATE, 2-MeO EMATE, 2 EtEMATE, and/or 2-MeO2bis EMATE, caused apoptosis of breast cancer cells in vitro, and activated caspases 3 and 8. Co-treatment with TRAIL increased apoptosis of the cells, and co-treatment with TRAIL also enhanced activation of capsase 3. The effects of co-administration with the oestrone compounds and TRAIL appear to be synergistic, and therefore, the *in vitro* data indicate that the composition could be used to treat a subject with estrogen dependent breast cancer, which would enable the composition. However, as discussed above, *in vivo* experiments demonstrate that treatment with EMATE results in increased levels of estrogen, and so is counter-indicated for treatment. Therefore, the specification and prior art are not enabling for the composition.

Even if the instant application were enabling for a composition comprising a TRAIL receptor ligand and a steroidal sulphamate compound having a sulfamate group attached to the 3 position of the A ring, it would not reasonably provide enablement for a composition comprising a steroidal sulphamate compound having a sulfamate group attached to a different position of the A ring or a different ring or having the substitutions recited in the claims, or a non-steroidal sulphamate compound. The specification does not enable any person skilled in the art to which

it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants have amended the claims to encompass a TRAIL ligand, and the rejection is overcome with regard to "any apoptosis inducer". Applicants traverse the rejection over non-steroidal sulphamate compounds and point to page 20, line 16 to page 21, line 1, in which is provided a non-steroidal skeletal structure, and submit that the amended claims now require that the sulphamate compound be a polycyclic compound. Applicants cite *In re Wands*, and assert that the skilled artisan is not without sufficient guidance to select compounds which can be used to practice the invention, and the quantity of experimentation would be low as a result of the high level of skill in the art, the state of the prior art, the large quantity of knowledge that exists as to compounds that are useful in the treatment of cancers, the significant amount of guidance provided in the specification, and the breath of the claims.

Applicants' arguments have been fully considered but are not deemed persuasive. Though the specification discloses a non-steroidal structure for sulfamate compounds, there were no experiments in which such a compound were tested for activity. Although testing such compounds and other polycyclic compounds may not necessarily be undue, the issue is that it is not predictable that these non-steroidal sulfamate compounds, or even steroidal sulfamate compounds with the recited substitutions, would have the same activities as the highly analogous compounds EMATE, 2-MeO EMATE, 2 EtEMATE, and 2-MeO2bis EMATE, such as binding oestrone sulfatase. Biological interactions, such as receptor-ligand binding and enzyme-substrate activity are very specific, requiring specific three-dimensional structures for proper interaction.

The state of the prior art provides evidence for, and is directly proportional to, the level or degree of predictability in the art. *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970). MPEP §§ 2164.03, 2164.05(a). In other words, the more that is known by one of ordinary skill in the art at the time the application was filed about the subject matter to which the claimed invention pertains, including how to make and use the invention, the higher the level or degree of predictability in the art. *Chiron Corp. v. Genentech Inc.*, 70 USPQ 2d 1321, 1326 (Fed. Cir. 2004). Therefore, the level or degree of "predictability or a lack thereof" in the art refers to the ability of one skilled in the art to extrapolate and thus readily anticipate the effect of a change within the disclosed subject matter to which the claimed invention pertains. *In re Marzocchi*, 169 USPQ 367, 369-70 (CCPA 1971). On the other hand, if one of ordinary skill in the art cannot readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is a lack of predictability in the art. See *In re Marzocchi* at pages 369-370.

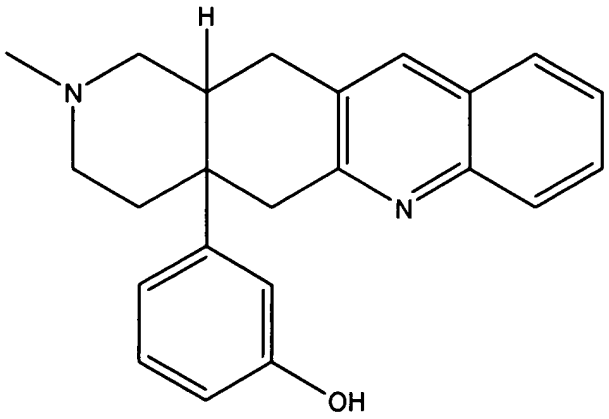
While a disclosure of each and every operable species claimed is not required, in patent applications containing claimed subject matter that is directed to the biotechnology, chemical and pharmaceutical arts, where the results are unpredictable, the disclosure within the specification of a few highly related species usually does not provide an adequate basis to support the generic claims, as more is typically required. *In re Vickers*, 61 USPQ 122, 127 (CCPA 1944); and *In re Fisher*, at 24. This is particularly the case when it is not readily apparent from the disclosure of a particular species, what other species will work. MPEP §§ 2164.03.

Drug discovery remains extremely tedious, laborious and expensive. For example, it is not all that uncommon for a pharmaceutical company to spend over one billion dollars in research and development, as well as clinical testing, before even a single drug sees the light of day in the marketplace, only then allowing said company the opportunity to begin recouping their investments for not only the successful drug, but also the countless other drugs that failed. Despite recent advancements in the sophistication of drug discovery instrumentation and techniques, an extraordinary degree of unpredictability still remains in the biotechnology, chemical and pharmaceutical arts, therefore requiring continued trial and error experimental research. The basis for the extraordinary degree of unpredictability associated with drug discovery in particular, can be attributed to the exquisite stereospecificity that exists between an enzyme and its corresponding substrate, or a ligand and its corresponding receptor. This principle is particularly evidenced by the following examples previously documented in the biotechnology, chemical and pharmaceutical scientific literature and prior art.

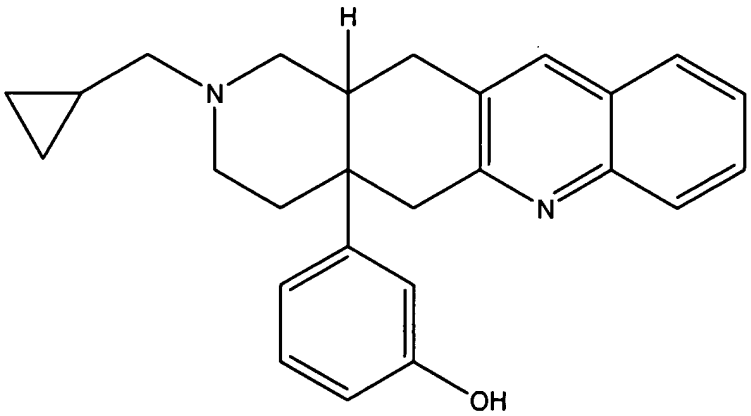
It is known in the biotechnology art that aminoacyl-tRNA synthetases exhibit an extremely high degree of stereospecificity with respect to their ability to discriminate between D- and L-optical isomers and between amino acids that are simple one carbon homologs of one another (i.e., aspartic acid versus glutamic acid), as well as between amino acids that are simply molecular isomers (i.e., leucine versus isoleucine)." Francklyn, C., Aminoacyl-tRNA Synthetases: Versatile Players in the Changing Theater of Translation, RNA, Vol. 8, pp. 1363-1372 (2002). It is also known that vertebrate growth hormone, which consists of 198 amino acids in length, transforms from being an agonist to an antagonist when a single amino acid is changed. U.S. Patent Number 5,350,836, which issued to Kopchick, et al. on September 27,

1994. It is further known that a majority of key therapeutics specifically act on particular cell surface receptors, for example: migraine drugs act on dopaminergic receptors; allergy drugs act on histamine receptors; asthma and blood pressure drugs act on adrenergic receptors; anti-depressive and anti-compulsive drugs act on serotonin receptors; and anti-anxiety drugs act on both serotonin receptors, as well as GABA receptors. For a general overview of the aforementioned cell surface receptors, see the relevant chapters and subheadings within Goodman & Gilman's The Pharmacological Basis of Therapeutics, 9th Ed., McGraw-Hill, NY, (1996).

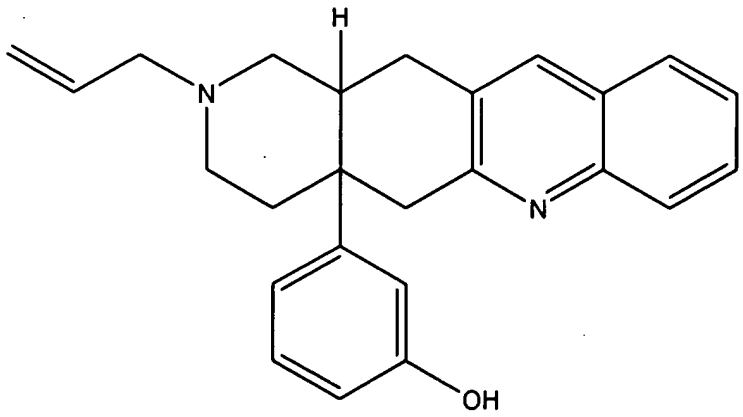
The unpredictable and surprisingly dramatic effects that can result from a simple modification of even a single pendant chemical moiety of an active core compound is strikingly apparent when considering opioid analgesics, for example. Upon simple substitution of the N-methyl group of TAN-67 (illustrated hereinbelow), which is a highly selective and potent nonpeptidic δ opioid receptor *agonist*, with either a methylcyclopropyl group, or even an allyl group for that matter, TAN-67 is subsequently converted into a δ opioid receptor *antagonist*! Goodman & Gilman's The Pharmacological Basis of Therapeutics, 9th Ed., McGraw-Hill, NY, page 549 (1996); and Nagase, H., et al., The Pharmacological Profile of δ Opioid Receptor Ligands, (+) and (-) TAN-67 on Pain Modulation, Life Sciences, Vol. 68, pp. 2227-2231 (2001).



3-(1,2,3,4,4a,5,12,12a-octahydro-2-methylpyrido[3,4-*b*]acridin-4a-yl)phenol (a.k.a. TAN-67)
delta opioid receptor ***agonist***

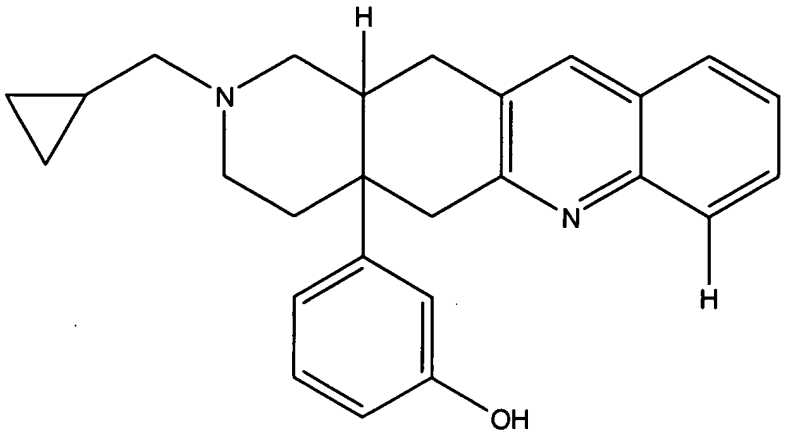


3-(2-(cyclopropylmethyl)-1,2,3,4,4a,5,12,12a-octahydropyrido[3,4-*b*]acridin-4a-yl)phenol
delta opioid receptor ***antagonist***

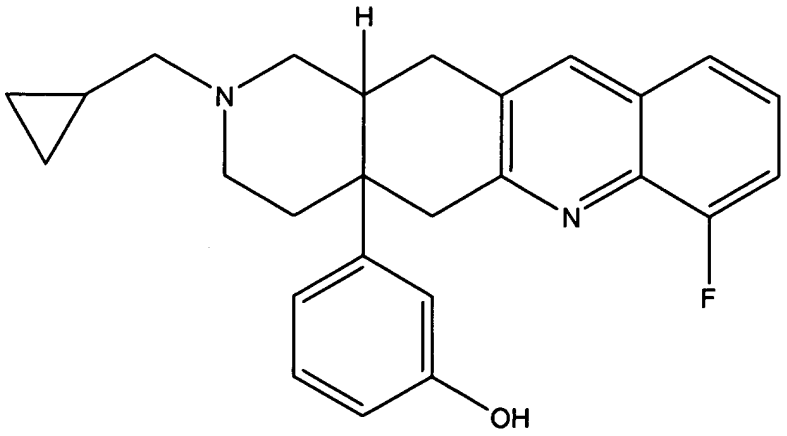


3-(2-allyl-1,2,3,4,4a,5,12,12a-octahydropyrido[3,4-*b*]acridin-4a-yl)phenol
delta opioid receptor ***antagonist***

In addition, if one were to modify the methylcyclopropyl substituted TAN-67, which is a δ opioid receptor *antagonist*, by substituting a fluorine atom for a hydrogen atom on the aromatic phenyl ring near the quinoline nitrogen (illustrated hereinbelow), the δ opioid receptor *antagonist* would be converted into a *partial* δ opioid receptor *agonist*, even though fluorine and hydrogen have the same atomic radius!!

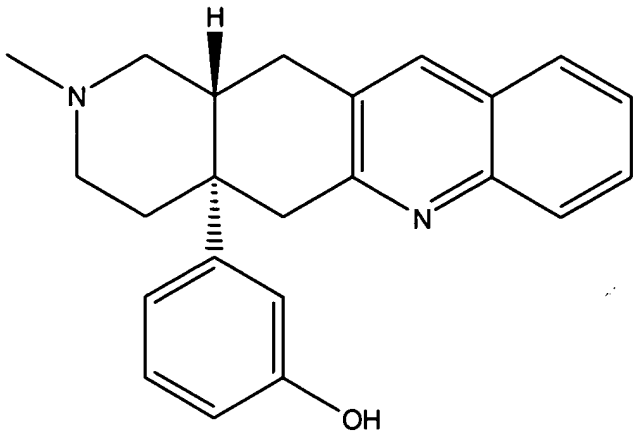


3-(2-(cyclopropylmethyl)-1,2,3,4,4a,5,12,12a-octahydropyrido[3,4-*b*]acridin-4a-yl)phenol
delta opioid receptor ***antagonist***

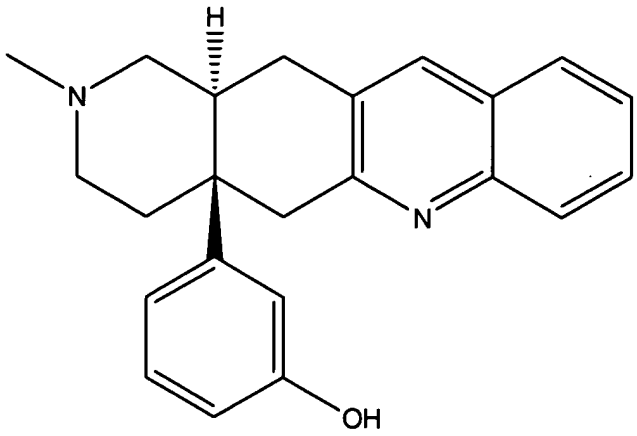


3-(2-(cyclopropylmethyl)-7-fluoro-1,2,3,4,4a,5,12,12a-octahydropyrido[3,4-*b*]acridin-4a-yl)phenol
partial delta opioid receptor ***agonist***

Moreover, by simply selecting from different stereoisomers of TAN-67 (illustrated hereinbelow), one could go from (-)TAN-67, which is a potent antinociceptive (analgesic), to (+)TAN-67, which not only fails to exhibit analgesic properties, but astonishingly induces pain-like nociceptive behavior, such as scratching and biting!



3-((4a*S*,12a*R*)-1,2,3,4,4a,5,12,12a-octahydro-2-methylpyrido[3,4-*b*]acridin-4a-yl)phenol
(a.k.a. (-)TAN-67)
potent antinociceptive (analgesic)



3-((4a*R*,12a*S*)-1,2,3,4,4a,5,12,12a-octahydro-2-methylpyrido[3,4-*b*]acridin-4a-yl)phenol
(a.k.a. (+)TAN-67)
induces pain-like nociceptive behavior

Based on the aforementioned discussion regarding opioid analgesics, it is readily apparent that minor, seemingly trivial, modifications to the core compound can create profound changes in biological activity. The paramount and unpredictable ramifications that minor structural modifications to the core compound can have on the biological activity of opioid receptors are equally pertinent and applicable to the development of agonists and antagonists of all receptors. Therefore, this example illustrates the exquisite stereospecific characteristics associated with all therapeutic receptor agonists and antagonists.

A final example evidencing unpredictability in association with drug discovery is illustrated by the following research efforts, which utilized combinatorial chemistry techniques. Combinatory chemistry is generally defined as a branch of applied chemistry concerned with the rapid synthesis and screening of large numbers of different but related chemical compounds generated from a known building block in order to recover new substances optimally suited for a specific function. In this particular example, combinatorial chemistry techniques were implemented in an effort to identify more efficacious inhibitors of cathepsin D, which is an aspartyl protease. Kick, E.K., et al., Structure-Based Design and Combinatorial Chemistry Yield Low Nanomolar Inhibitors of Cathepsin D, Chemistry & Biology, Vol. 4, No. 4, pp. 297-307 (1997). More specifically, combinatorial libraries were designed and created around the synthesis and subsequent structural derivatization of a stable mimetic building block of the tetrahedral intermediate of amide hydrolysis, namely (hydroxyethyl)amine isostere, which was an already known inhibitor of aspartyl proteases. Of the 2,000 derivatives that comprised the resultant and expansive library, over 90% of the synthesized compounds were biologically *inactive*. Since more than 90% of the synthesized compounds generated in the aforementioned

combinatorial library, which was designed and created around the structural derivatization of a stable and efficacious building block or active core, were in fact biologically *inactive*, one of ordinary skill in the art would have a justifiably sound reason to doubt that even a reasonable fraction, much less a simple majority, of the chemical derivatives disclosed across the entire scope of the tremendously broad and extremely generic claims would in fact possess desired biological activity. With such a high degree of unpredictability in the drug discovery art, the applicant bears a greater burden of providing adequate support in the specification so as to guide one of ordinary skill in the art through the generic maze that is commensurate in scope with the claims.

In general, the basis for the extraordinary degree of unpredictability associated with all of the previously discussed unexpected scientific experimental results can be directly attributed to the stereospecificity that exists between an enzyme and its corresponding substrate, and a ligand and its corresponding receptor. As a result, one of ordinary skill in the art would not be able to reasonably predict or anticipate the ramifications that minor structural changes, can have on the bioactive properties thereof.

Regarding the activity of compounds on oestrone sulfatase, Kasch et al., U.S. Patent No. 6,339,079, teaches that the pharmacological effect of estradiol sulfamate compounds can be specifically changed depending on the substitution pattern, which makes it possible to use them as sulfatase inhibitors on the one hand and as estrogen components on the other hand (column 1, line 50 to column 2, line 58).

Therefore, one of ordinary skill in the art would not expect that any polycyclic sulfamate compound, which could have any number or arrangement of rings, would bind oestrone

sulfatase. EMATE is identical to oestrone except for replacement of the hydroxyl at position 3 on ring A of oestrone with a sulfamate group. The skilled artisan would expect that the steroid structure is critical for binding the oestrone sulfatase. It is also readily apparent that one of ordinary skill in the art would not be able to accurately extrapolate how minor structural changes of various chemical substituents associated with the disclosed active steroid sulfamates would affect the inhibitory characteristics thereof. In conclusion, due to the three-dimensional constraints on interacting molecules and the high degree of unpredictability in the art at the time the instant application was filed with respect to accurately extrapolating how major structural changes (steroid to polycyclic) or minor structural changes of various chemical substituents can dramatically affect the inhibitory characteristics thereof, one of ordinary skill in the relevant art would not be able use the invention commensurate in scope with the aforementioned rejected claims.

Conclusion

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (571) 272-0878. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached at (571) 272-0829.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://portal.uspto.gov/external/portal/pair. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Eileen B. O'Hara

EILEEN B. O'HARA
PATENT EXAMINER

Eileen B. O'Hara, Ph.D.

Patent Examiner

George C. Elliott

DIRECTOR
TECHNOLOGY CENTER 1600